REMARKS

Applicant respectfully requests reconsideration. Claims 1-5, 12-17, 22, 24-28, 32, 36, 39, 44, 46, 48, 49, 66, 67, and 95-100 were previously pending in this application. No claims are amended herein. As a result, claims 1-5, 12-17, 22, 24-28, 32, 36, 39, (44), 46, 48, 49, 66, 67, 95-99 and (100) are still pending for examination, with claims 1, (44), 49, 66, 67, 97 and 98 being independent claims (See remarks below for claims 44 and 100). Claims 1, 2, 12, 14, 16, 17, 22, 24, 26, 27, (44), 49, 66, 67, 97, 98 and (100) represent elected species (See remarks below for claims 44 and 100). No new matter has been added.

Elected Claims Under Examination

It is noted that as a result of the Restriction Requirement set forth in the Office Action mailed June 30, 2006, and the subsequent election of Group I dated July 28, 2006, claims 1-5, 12-17, 22, 24-28, 32, 36, 39, 44, 46, 48-49, 66-67, 70, 88, 94-99 and 100 are pending for examination in this application; however, the Office Action of June 22, 2007, appears to erroneously omit claim 100 (Office Action Summary Sheet, under Disposition of Claims # 4; on page 2, under Election/Restrictions # 4). It is also noted that claim 100 appears to be included in substantive examination.

It is also noted that claim 44 is indicated by the Examiner to be both an elected species *and* non-elected species (Office Action page 2, under Election/Restrictions). Claim 44 does not appear to be substantively examined, and it is not listed as a rejected claim under 35 USC 102 (page 4).

Clarification for the status of the aforementioned claims 44 and 100 is respectfully requested.

Rejection Under 35 U.S.C. 102

Claims 1-2, 12, 14, 16-17, 22, 24, 26-27, 49, 66-67, 97-98 and 100 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Krieg et al. WO 01/22972 A2 ("Krieg et al."). Applicant respectfully disagrees for the following reasons.

Initially, it is noted that much of the rejection presented in the Office Action under 102(b) appears in fact to cite the instant application, not the cited reference. Specifically, Applicant calls to the Examiner's attention that the first full paragraph on page 5 of the Office Action, beginning as "Krieg et al teaches..." actually quotes from the specification of the instant application, although provided as support for anticipation. Similarly, the paragraph immediately following the aforementioned paragraph (i.e., first full paragraph on page 6), also refers to the instant application, including the cited page numbers. Furthermore, the last paragraph of the Claim Rejections Section on page 8 also describes the instant invention, not the cited reference. The fact that the instant invention and the PCT publication cited by the Examiner under 102(b) share a common inventor, Krieg, may have contributed to the error. Notwithstanding, Applicant's arguments are presented below to assert that Krieg et al. does not anticipate the invention of the instant application.

Krieg et al. does not anticipate the claimed invention because the cited reference does not teach each element of the instant claims. Instant claim 1 is drawn to an immunostimulatory nucleic acid molecule having at least one internal pyrimidine-purine (YZ) dinucleotide and a chimeric backbone, wherein the at least one internal YZ dinucleotide has a phosphodiester or phosphodiester-like internucleotide linkage, wherein optionally each additional internal YZ dinucleotide has a phosphodiester, phosphodiester-like, or stabilized internucleotide linkage, and wherein all other internucleotide linkages are stabilized.

An important finding of the instant invention relates to the discovery that a phosphodiester or phosphodiester like internucleotide linkage can be present between the C and G of the CpG motif without causing a significant loss in activity. At the time of the invention it was believed phosphorothioate stabilized oligonucleotides were more stable than phosphodiester oligonucleotides. Further it was expected that placing a phosphodiester internucleotide linkage between the C and G in the CpG motif of an oligonucleotide might reduce the activity of an immunostimulatory oligonucleotide because it was believed that the oligonucleotide might be more susceptible to breakage at the phosphodiester linkage between the C and G nucleotides, producing smaller oligonucleotides without a CpG motif. Surprisingly, however, it was discovered that placing a phosphodiester (also referred to as a soft linkage) between the C and G in an otherwise phosphorothioate oligonucleotide did not result in a loss of activity. In some instances better

activity was observed with these molecules. Krieg et al does not describe such molecules, having a phosphodiester or phosphodiester-like linkage between the C and G of the CpG motif. As far as applicant is aware, Krieg et al does not provide any specific examples of such a molecule.

Krieg et al. generally relates to methods of stimulating immune response using a Py-rich or T-rich immunostimulatory nucleic acid and a TG nucleic acid. Krieg et al. teaches various immunostimulatory nucleic acid compositions, including Py-rich, T-rich in particular, poly T (e.g., TTTT), and TG nucleic acids. The Krieg reference teaches generally that such immunostimulatory nucleic acid may have chimeric backbones (See, for example, page 8, line 13). No guidance, however, is provided for placing a phosphodiester or phosphodiester-like linkage between the C and G of the CpG motif.

The cited reference also discloses some embodiments wherein an immunostimulatory nucleic acid having an unmethylated CG dinucleotide, TG dinucleotide or Py-rich sequence "has a completely phosphodiester backbone" (page 11, line 1), while in other embodiments it has "a modified backbone" (page 11, line 3). Krieg et al. teaches that "nucleic acid stabilization can be accomplished via phosphate backbone modifications" (page 36, first paragraph). The reference further teaches that "at least a partial modified backbone" can be used and that in some cases "combinations" of phosphodiester and phosphorothioate among others can be used (page 36). Furthermore, the specification of the cited reference teaches that, "the center nucleotides (N_1ZN_2) of the formula $Y_1N_1ZN_2Y_2$ have phosphodiester internucleotide linkages and Y_1 and Y_2 have at least one modified internucleotide linkage" (page 9, first full paragraph; also on page 37, second paragraph), where Z represents an immunostimulatory nucleic acid motif *excluding* a CG. The reference teaches that the central nucleotides (N_1ZN_2) has at least 6 nucleotides (page 8, line 22). Thus, the cited reference, while providing embodiments having chimeric backbones, does not specifically provide the limitation that the pyrimidine-purine dinucleotide is linked via a phosphodiester or phosphodiester-like linkage, as provided in the instantly claimed invention. Because the limitation of the claimed invention is missing in the teaching of Krieg et al., the cited reference is not anticipatory. In addition, claims 2, 12, 14, 16, 17, 22, 24, 26 and 27, which depend from claim 1, are also novel over the reference for the same reasons stated above.

Similarly, claims 49 and 66 are also novel over Krieg et al. because the instant claims include the limitation that the internucleotide linkage between the pyrimidine-purine dinucleotide motif (e.g., YZ and CG) is a phosphodiester or phosphodiester-like internucleotide linkage, and the oligonucleotide includes at least one stabilized internucleotide linkage. Krieg et al. does not teach these limitations.

Claim 67 is also novel over Krieg et al. because Krieg et al. fails to provide all elements of the instant claim. Claim 67 is drawn to an oligonucleotide comprising 5'GNC 3', wherein N is a nucleic aid sequence of 4-10 nucleotides in length and is at least 50% T and does not include a CG dinucleotide, and the oligonucleotide includes at least one stabilized internucleotide linkage. On the other hand, Krieg et al. teaches the formula $Y_1N_1ZN_2Y_2$ having phosphodiester internucleotide linkages and Y_1 and Y_2 having at least one modified internucleotide linkage (page 9, first full paragraph; also on page 37, second paragraph), and where Z represents an immunostimulatory nucleic acid motif (TTTT, TG, or a sequence having at least 50% Ts) excluding a CG. The cited reference further teaches that the central nucleotides (N_1ZN_2) have at least 6 nucleotides (page 8, line 22). According to the teaching of the cited reference, therefore, a sequence of the formula $Y_1N_1ZN_2Y_2$ is at least 8 nucleotides in total length. In contrast, the instant invention teaches that an oligonucleotide comprising 5'GNC 3' is in the range of 6-12 nucleotides in length, given that N is 4-10 nucleotides in length. In addition, whereas Krieg et al. teaches that the nucleotides of the N_1ZN_2 motif have a phosphodiester backbone, the reference does not specify that the internucleotide linkage between a pyrimidine-purine dinucleotide (e.g., wherein Z is a TG) is a phosphodiester linkage and that the oligonucleotide includes at least one stabilized internucleotide linkage. Therefore, Krieg et al. does not anticipate instant claim 67.

The Examiner further rejected claims 66 and 100 as being anticipated by Krieg et al. The subject claims are drawn, each in pertinent part, to the sequence, TCGTCGTTTTGACGTTTTGTCGTT, with additional limitations regarding internucleotide linkages. Applicant notes that the sequence is provided in Krieg et al but only in the context of phosphorothioate-modified oligonucleotide. This sequence corresponds to SEQ 343 of Table A as described in Krieg et al., which indicates that the oligonucleotide is "stabilized" as opposed to "chimeric." Example 12 of Krieg et al. further indicates that the ODNs used in these studies were

"phosphorothioate ODN" including ODN 2102, which has the sequence of SEQ ID NO:343 as noted above. Therefore, this oligonucleotide, as disclosed in Krieg et al., does not include each and every limitation of the instant claims and thus does not anticipate instant claims 66 and 100.

As noted earlier, Applicant respectfully contends that the last paragraph under Claim Rejections (page 8) also describes limitations of the instant invention, *not* the cited Krieg et al. reference. Applicant is not aware of a teaching in Krieg et al. that anticipates claims 66, 97, 98 and 100.

In view of the foregoing, Krieg et al. does not anticipate the claimed invention. Accordingly, it is respectfully requested that the rejections made under § 102(b) be withdrawn.

Double Patenting Rejection

Claim 49 has been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Application No. 11/361,313.

Applicant respectfully requests that this rejection be held in abeyance since the co-pending claim has not yet been allowed. Applicant notes that the instant claims have an earlier priority date. If in fact a double patenting rejection is appropriate, which applicant does not agree with, the earlier filed claims should be allowed and the rejection should be made in the later filed application.

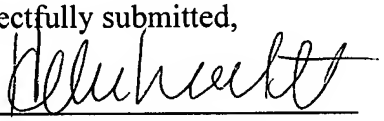
CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Dated: December 14, 2007

Respectfully submitted,

By 

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